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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/645,654	08/20/2003	Ihor Shevchuk	6750-130-999	8830

20583 7590 04/30/2007

JONES DAY
222 EAST 41ST ST
NEW YORK, NY 10017

EXAMINER	
GHALI, ISIS A D	
ART UNIT	PAPER NUMBER
1615	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/30/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/645,654	SHEVCHUK ET AL.	
	Examiner	Art Unit	
	Isis A. Ghali	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 February 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The receipt is acknowledged of applicants' request for reconsideration filed 02/05/2007.

Claims 1-35 are pending and included in the prosecution.

The following rejections have been discussed in the previous office action, and are maintained for reasons of record:

Specification

1. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Response to Arguments

2. Applicants have not indicated review of the specification for possible errors. Therefore, the objection previously made to the specification is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,149,538 ('538).

US '538 teaches transdermal delivery patch form comprising opioid analgesics and one or more antagonists for said opioid in an effective amount to attenuate the euphoric effect of said opioid if the patch is tampered with (abstract; col.3, lines 42-43). The preferred opioid is buprenorphine and the preferred antagonist is naltrexone (col.2, lines 65-68). Opioid analgesics include buprenorphine, fentanyl, oxycodone, and pharmaceutically acceptable salts thereof (col.4, lines 31-52). The patch comprises one

or more antagonists including naltrexone, naloxone, nalmefene, cyclazocine, pharmaceutically acceptable salts thereof, and mixtures thereof (col.5, lines 26-39). The patch is reservoir or matrix type, gel, cream or paste (col.4, lines 10-11, 63-64).

US '538 does not explicitly teach the presence of the free base antagonist and its salt in the patch and their amounts and ratios. The reference does not teach a kit comprising the transdermal patch and printed instruction on how to use the kit.

US '538 suggests combination of one or more opioid analgesics and combination of one ore more antagonists including the antagonist, i.e. free base, and their salts. A conclusion of obviousness under 35 U.S.C. 103 (a) does not require absolute predictability, only a reasonable expectation of success; and references are evaluated by what they suggest to one versed in the art, rather than by their specific disclosure. *In re Bozek*, 163 USPQ 545 (CCPA 1969). Therefore, it would have been obvious to one having ordinary skill in the art at he time of the invention to provide transdermal patch comprising opioid analgesic and antagonist in the free base or salt form as disclosed by US '538, and use both the free base and salt of the antagonist motivated by the knowledge available to the skilled artisan that salts and free bases of the drugs have different solubility and bioavailability and combination of both will provide different release time providing prolonged period of release instead of having the antagonist in one form that has the same release period, with reasonable expectation of having the transdermal patch comprising opioid analgesic and antagonist in the free base and in the salt form to provide prolonged release of the antagonist all through the use time of the device.

Regarding the claimed amounts and ratios, the references do not specifically teach the ingredients in the amounts claimed by applicant. The amount of a specific ingredient in a composition is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. It would have been customary for an artisan of ordinary skill to determine the optimal amount of each ingredient in order to best achieve the desired results. Thus, absent some demonstration of unexpected results from the claimed parameters, this optimization of ingredient amount would have been obvious at the time of applicant's invention. One having ordinary skill in the art would have determined the amount of the opioid and its antagonist according to specific patient need and severity of pain. One having ordinary skill in the art would have adjusted the ratio between the salt and free base of the antagonist according to their solubility and bioavailability of the salt and free base of each antagonist to obtain continuous antagonistic effect as well as effective pain relieve.

Regarding printed instruction, it is a routine work for all the available pharmaceuticals and cosmetics, and one having ordinary skill in the art would always includes a printed instruction with any pharmaceutical product to ensure effective non-hazardous use of the pharmaceuticals.

Therefore, the invention as whole is *prima facie* obvious in view of US '538.

Response to Arguments

5. Applicant's arguments filed 02/05/2007 have been fully considered but they are not persuasive. Applicants traverse the obviousness rejection over Granger by arguing that:

- Granger teaches transdermal device comprising opioid and opioid antagonist wherein the opioid and its antagonist are physically separated by impermeable barrier that precludes the delivery of the antagonist under normal usage. In the present invention the antagonist can be present any where in the matrix.

In response to these arguments, applicants' attention is directed to the scope of the present claims that is directed to a transdermal device comprising active agent and its antagonist in the form of mixture of free base and salts, and all the elements of the device are disclosed or suggested by Granger. The expression "comprising" of the claims' language permits the presence of other elements such as the impermeable barrier. The antagonist disclosed by the reference is also present any where in the matrix. Regarding applicants argument that the barrier preclude the delivery of the antagonist under normal usage, such a limitation is directed to the intended use of the device, and it does not impart patentability to the claims. The recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In any event, such intended use is not even recited by the claims.

- Applicants argue that Granger is silent regarding the use of combination of antagonist in the form of free base and salts. The antagonist of the present invention diffuses out of the matrix in an amount insufficient to inhibit the analgesic effect of the active agent.

In response to this argument, it is argued that the use of patents as references is not limited to what the patentees describe as their own inventions or to the problems with which they are concerned. They are part of the literature of the art, relevant for all they contain. *In re Heck*, 699 F.2d 1331, 1332—33, 216 USPQ 1038, 1039 (Fed. Cir 1983). A reference may be relied upon for all that it would have reasonable suggested to one having ordinary skill in the art, including nonpreferred embodiments. Granger at col.5, lines 26-39, teaches the antagonists, either free base form or salt form, and in particular at lines 36-38, Granger teaches mixture thereof. Granger teaches and suggests the combination and mixtures of the antagonists in the free base form and their salts. A conclusion of obviousness does not require absolute predictability, but reasonable expectation of success, and the references are evaluated by what they have suggested to one versed in the art, rather than by their specific disclosure. The rationale to modify the prior art does not have to be expressly stated in the prior art; the rationale may be expressly or impliedly contained in the prior art or it may be reasoned from knowledge generally available to one of ordinary skill in the art and the reason to modify the reference may often suggest what the applicant has done.

- Applicants argue that in the present invention the delivery rate of antagonist combination is partially controlled by the rare of the diffusion of the antagonist out of the matrix.

In response this argument, it is noted that the features upon which applicant relies (i.e., the delivery rate of antagonist combination is partially controlled by the rare of the diffusion of the antagonist out of the matrix) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

- Applicants argue that there is no suggestion in Granger that the antagonist combination could be used in transdermal patch without the use of the barrier separating the active agent and its antagonist. Granger fails to teach all the claimed limitation and fails to establish prima facie case of obviousness.

In response to this argument, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir.1992). In this case, Granger suggested mixture of antagonist and their salts, and it would have been obvious to one having ordinary skill in the art at he time of the invention to provide transdermal patch comprising opioid analgesic and antagonist in the free base or salt form as disclosed by US '538, and use both the free base and salt of the antagonist motivated by the knowledge available to the skilled artisan that salts and free bases of the drugs have different solubility and bioavailability and combination of both will provide

different release time providing prolonged period of release instead of having the antagonist in one form that has the same release period, with reasonable expectation of having the transdermal patch comprising opioid analgesic and antagonist in the free base and in the salt form to provide prolonged release of the antagonist all through the use time of the device. Therefore, one having ordinary skill in the art would have modified the disclosure of Granger to achieve the present invention. In considering the disclosure of the reference, it is proper to take into account not only the specific teachings of the reference but also the inferences which one skilled in the art would reasonably be expected to draw therefrom. *In re Preda*, 401 F.2d 825, 826, 159 USPQ 342, 344 (CCPA 1968). The rational to modify or to combine the prior art does not have to be expressly stated in the prior art; the rational may be expressly or impliedly contained in the prior art or it may be reasoned from knowledge generally available to one of ordinary skill in the art. The reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve different problem. It is not necessary that the prior art suggest the combination or modification to achieve the same advantage or result discovered by applicant. *In re Linter*, 458 F.2d 1013, 173 USPQ 560 (CCPA 1972).

In the light of the foregoing discussion, the Examiner's ultimate legal conclusion is that the subject matter defined by the claims would have been prima facie obvious within the meaning of 35 U.S.C. 103 (a).

Conclusion

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Isis Ghali whose telephone number is (571) 272-0595. The examiner can normally be reached on Monday-Thursday, 7:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Isis Ghali
Examiner
Art Unit 1615

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ISIS GHALI
PRIMARY EXAMINER